

NMCP COVID-19 Literature Report #64: Friday, 26 March 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

Changes of Note

The [first NMCP COVID-19 literature report](#) came out a year ago. Since then, these reports have evolved from a few pages with a handful of articles and reports to 30+ pages with various sections that barely scratch the surface of what COVID-19 related literature is out there. To keep them relevant and useful, you will notice some changes (big and small) starting with this report, including:

- Shifting to updates and releases every other week (the next will be Friday, 09 April 2021)
- Reorganizing sections and grouping news, articles, and special reports by topic rather by date published
- A table of contents and internal links to sections to aid in finding what's most relevant to you
- Leaving off preprints except as part of news items (see [COVID-19 SARS-CoV-2 preprints](#) from [medRxiv](#) and [bioRxiv](#) if you want those)
- Listing citations (which are important!) on the website instead of within the report to keep the length manageable (although links to sources will remain)
- The website will remain private (see: <https://nmcp.libguides.com/covidreport>) but will no longer require a password

I hope these reports continue to be useful and of value to you. Please reach out with suggestions, ideas for topics, or other constructive feedback.

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The Big Picture

News in Brief

"Covid: The countries that nailed it, and what we can learn from them" ([BBC](#)).

"Has COVID peaked? Maybe, but it's too soon to be sure: Global COVID-19 cases have fallen significantly since they peaked in early January. Scientists are asking whether this is the beginning of the end of the pandemic." ([Nature](#))

"The future of the pandemic in the US: experts look ahead" ([NPR](#)).

Long read: "How the west lost COVID: How did so many rich countries get it so wrong? How did others get it so right?" ([Intelligencer](#)).

SARS-CoV-2 Variants

News in Brief

"What you need to know about the coronavirus variants" ([WashPo](#)).

"What happens when a person is simultaneously infected with two different SARS-CoV-2 variants?" ([Global Biodefense](#))

"The coronavirus variants don't seem to be highly variable so far" ([SciAm](#)).

"Rare COVID reactions might hold key to variant-proof vaccines" ([Nature](#)).

Peer-Reviewed Articles

NEJM: [New SARS-CoV-2 Variants — Clinical, Public Health, and Vaccine Implications](#) (24 March 2021)

"Three new variants that have rapidly become dominant within their countries have aroused concerns: B.1.1.7, 501Y.V2, and P.1. All three variants have the N501Y mutation, which changes the amino acid asparagine (N) to tyrosine (Y) at position 501 in the receptor-binding domain of the spike protein. Four key concerns stemming from the emergence of the new variants are their effects on viral transmissibility, disease severity, reinfection rates (i.e., escape from natural immunity), and vaccine effectiveness (i.e., escape from vaccine-induced immunity)." (summary from [JHCHS newsletter](#))

JAMA: [Neutralizing Antibodies Against SARS-CoV-2 Variants After Infection and Vaccination](#) (19 March 2021)

"This study examines the neutralizing antibody response to 4 SARS-CoV-2 variants in infected and vaccinated individuals."

Euro Surveill: [Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16 November to 5 February](#) (18 March 2021)

"The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of concern B.1.1.7 (VOC) was first identified in Kent, United Kingdom (UK) in autumn 2020. Early analysis suggests it is more transmissible than previously circulating forms (non-VOC). It is now the dominant strain throughout the UK and is increasing in prevalence across Europe. Early reports of increased mortality have not included data on individuals' comorbidities, and this information is needed to facilitate pandemic planning.

Certain PCR assays for SARS-CoV-2 do not amplify one of the spike protein gene targets in this VOC. Spike gene target failure (SGTF) is therefore a proxy for VOC identification, with

greater than 95% sensitivity for VOC diagnosis during the period from 16 November to 11 January.

Working on behalf of NHS England, we estimate the risk of death following confirmation of SARS-CoV-2 infection in England, comparing infection with VOC to non-VOC, after accounting for demographic factors and comorbidities. The code and configuration of our analysis is available online (github.com/opensafely/sgtf-cfr-research)."

NEJM: [Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine](#) (17 March 2021)

"Protection conferred by the mRNA-1273 [Moderna] vaccine against the P.1, B.1.427/B.1.429, and B.1.351 variants remains to be determined. Our findings underscore the importance of continued viral surveillance and evaluation of vaccine efficacy against new variants and may help to facilitate the establishment of correlates of protection in both nonhuman primates and humans."

NEJM: [Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant](#) (16 March 2021)

"Assessment of the safety and efficacy of vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in different populations is essential, as is investigation of the efficacy of the vaccines against emerging SARS-CoV-2 variants of concern, including the B.1.351 (501Y.V2) variant first identified in South Africa.

We conducted a multicenter, double-blind, randomized, controlled trial to assess the safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) in people not infected with the human immunodeficiency virus (HIV) in South Africa. Participants 18 to less than 65 years of age were assigned in a 1:1 ratio to receive two doses of vaccine containing 5×10^{10} viral particles or placebo (0.9% sodium chloride solution) 21 to 35 days apart. Serum samples obtained from 25 participants after the second dose were tested by pseudovirus and live-virus neutralization assays against the original D614G virus and the B.1.351 variant. The primary end points were safety and efficacy of the vaccine against laboratory-confirmed symptomatic coronavirus 2019 illness (Covid-19) more than 14 days after the second dose.

Between June 24 and November 9, 2020, we enrolled 2026 HIV-negative adults (median age, 30 years); 1010 and 1011 participants received at least one dose of placebo or vaccine, respectively. Both the pseudovirus and the live-virus neutralization assays showed greater resistance to the B.1.351 variant in serum samples obtained from vaccine recipients than in samples from placebo recipients. In the primary end-point analysis, mild-to-moderate Covid-19 developed in 23 of 717 placebo recipients (3.2%) and in 19 of 750 vaccine recipients (2.5%), for an efficacy of 21.9% (95% confidence interval [CI], -49.9 to 59.8). Among the 42 participants with Covid-19, 39 cases (92.9%) were caused by the B.1.351 variant; vaccine efficacy against this variant, analyzed as a secondary end point, was 10.4%

(95% CI, -76.8 to 54.8). The incidence of serious adverse events was balanced between the vaccine and placebo groups.

A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate Covid-19 due to the B.1.351 variant."

Nature: [Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7](#) (15 March 2021)

"SARS-CoV-2 lineage B.1.1.7, a variant first detected in the UK in September 2020, has spread to multiple countries worldwide. Several studies have established that B.1.1.7 is more transmissible than preexisting variants, but have not identified whether it leads to any change in disease severity². Here we analyse a dataset linking 2,245,263 positive SARS-CoV-2 community tests and 17,452 COVID-19 deaths in England from 1 September 2020 to 14 February 2021. For 1,146,534 (51%) of these tests, the presence or absence of B.1.1.7 can be identified because of mutations in this lineage preventing PCR amplification of the spike gene target (S gene target failure, SGTF1). Based on 4,945 deaths with known SGTF status, we estimate that the hazard of death associated with SGTF is 55% (95% CI 39–72%) higher after adjustment for age, sex, ethnicity, deprivation, care home residence, local authority of residence and test date. This corresponds to the absolute risk of death for a 55–69-year-old male increasing from 0.6% to 0.9% (95% CI 0.8–1.0%) within 28 days after a positive test in the community. Correcting for misclassification of SGTF and missingness in SGTF status, we estimate a 61% (42–82%) higher hazard of death associated with B.1.1.7. Our analysis suggests that B.1.1.7 is not only more transmissible than preexisting SARS-CoV-2 variants, but may also cause more severe illness."

Vaccines and Vaccine Hesitancy

News in Brief

Some National Guard personnel transporting COVID-19 vaccines have been held up at gunpoint in Texas ([NBC](#)).

J&J's one-shot COVID vaccine is sparking confusion as millions of doses sit unused ([Politico](#)).

Moderna is starting a Phase 1 study for a new COVID-19 mRNA vaccine that will be refrigerator stable ([HPN](#)).

What's next for vaccines? Targeting for variants and lower cost – at least those are the goals ([Nat Biotech](#)).

AstraZeneca Concerns

There's been growing controversy surrounding the Oxford-AstraZeneca COVID vaccine as some countries paused rollout after concerns of increased blood clots and other adverse events with it ([CIDRAP](#)).

The mishaps and unforced errors are overshadowing the vaccine ([STAT](#)), leading the NIH to release a statement ([NIH](#)) that only added to the confusion and concerns about the data being outdated ([Endpoints](#); [STAT](#)).

Here is a good explainer: "What scientists do and don't know about the Oxford–AstraZeneca COVID vaccine: Results confirming the vaccine's strong protection against COVID-19 were welcomed following last week's pause in roll-outs — but fresh questions have now emerged about the data" ([Nature](#)).

Who Is (And Who Isn't) Getting Vaccinated

According to a recent poll of healthcare workers, 52% have gotten at least 1 dose of a COVID-19 vaccine, 19% plan to get one, 12% haven't decided, and 18% don't plan on getting vaccinated ([WashPo](#)).

"Who isn't getting vaccinated, and why: A new report highlights why different groups are hesitant to get the coronavirus vaccine and what can be done about it" ([Recode](#); see also: [full survey report \[pdf\]](#) from CMU).

It doesn't help matters that where you live and who you know might determine if you can get vaccinated ([NYT](#)).

Looking to celebrate after you get a COVID-19 vaccine? One sweet option: Krispy Kreme is giving away free doughnuts if you show your vaccination card ([USA Today](#)). This, of course, led to a bit of a dust storm about doughnuts as incentive ([Twitter](#)).

Peer-Reviewed Articles

JAMA Netw Open: [Trends in Health Care Worker Intentions to Receive a COVID-19 Vaccine and Reasons for Hesitancy](#) (23 March 2021)

"This survey study queried employees of a health care system before COVID-19 vaccine distribution to assess their intentions to receive a vaccine and to understand their reasons for hesitancy to do so."

NEJM: [SARS-CoV-2 Infection after Vaccination in Health Care Workers in California](#) (23 March 2021)

"University of California researchers evaluated COVID-19 infection rates in 36,659 HCWs on the San Diego and Los Angeles campuses vaccinated with at least one dose of the Moderna or Pfizer/BioNTech vaccine from Dec 16, 2020, to Feb 9, 2021. In that timeframe, 28,184 (77%) received the second dose of vaccine.

Of the 36,659 vaccinated HCWs, 379 (1.0%) tested positive for COVID-19 1 or more days after vaccination, 71% of them within the first 2 weeks after the first dose. Of the 28,184 HCWs who received their second dose, 37 (0.1%) tested positive, 22 of them 1 to 7 days later. Eight tested positive 8 to 14 days later, and 7 did so at least 15 days later.

With 5,455 HCWs at the San Diego campus and 9,535 at the Los Angeles campus who received their second vaccine dose at least 2 weeks before testing, the findings correspond to a 0.05% positivity rate. The absolute risk of infection after vaccination was 1.19% among San Diego HCWs and 0.97% among those in Los Angeles." (summary extracted from [CIDRAP](#))

MMWR: [COVID-19 Vaccine Second-Dose Completion and Interval Between First and Second Doses Among Vaccinated Persons — United States, December 14, 2020–February 14, 2021](#) (19 March 2021)

"What is already known about this topic? During December 2020, two 2-dose COVID-19 vaccines received Emergency Use Authorization from the Food and Drug Administration.

What is added by this report? Among persons who received a first dose and for whom sufficient time had elapsed to receive the second dose, 88.0% had completed the series; 8.6% had not received the second dose but were still within the allowable interval to receive it. Among all 2-dose recipients, 95.6% received the second dose within the recommended interval. Differences in missed doses or second doses administered outside the recommended interval were identified among jurisdictions and demographic groups.

What are the implications for public health practice? Identifying and addressing possible barriers to completing the COVID-19 vaccination series can help ensure equitable coverage across communities and optimal health benefits for recipients."

MMWR: [County-Level COVID-19 Vaccination Coverage and Social Vulnerability — United States, December 14, 2020–March 1, 2021](#) (17 March 2021)

"What is already known about this topic? COVID-19 has disproportionately affected racial/ethnic minority groups and persons who are economically and socially disadvantaged. Ensuring equitable COVID-19 vaccine coverage is a national priority.

What is added by this report? In the first 2.5 months of the U.S. vaccination program, high social vulnerability counties had lower COVID-19 vaccination coverage than did low social vulnerability counties. Although vaccination coverage estimates by county-level social vulnerability varied widely among states, disparities in vaccination coverage were observed in the majority of states.

What are the implications for public health practice? Continued monitoring of vaccination coverage by social vulnerability metrics is critical for developing tailored, local vaccine administration and outreach efforts to reduce COVID-19 vaccination inequities."

PNAS: [Vaccinating the oldest against COVID-19 saves both the most lives and most years of life](#) (16 March 2021)

"Many competing criteria are under consideration for prioritizing COVID-19 vaccination. Two criteria based on age are demographic: lives saved and years of future life saved. Vaccinating the very old against COVID-19 saves the most lives, but, since older age is accompanied by falling life expectancy, it is widely supposed that these two goals are in conflict. We show this to be mistaken. The age patterns of COVID-19 mortality are such that vaccinating the oldest first saves the most lives and, surprisingly, also maximizes years of remaining life expectancy. We demonstrate this relationship empirically in the United States, Germany, and South Korea and with mathematical analysis of life tables. Our age-risk results, under usual conditions, also apply to health risks."

Treatments and Management

News in Brief

Some patients are refusing ventilators because of fears that the machines will kill them ([WashPo](#)).

AstraZeneca will supply up to half a million doses of AZD7442, their antibody combination currently under investigation, to the US government ([HPN](#)).

Pfizer is starting a new early trial of a protease inhibitor (PF-07321332) as a possible oral therapy for COVID-19 ([Reuters](#)).

"COVID antibody treatments show promise for preventing severe disease – but uptake by patients and physicians has been low in the United States, where some therapies have been authorized for months" ([Nature](#); see also: [bioRxiv preprint](#)).

Podcast: [Why COVID antibody treatments may not be the answer](#) (19 March 2021)

Peer-Reviewed Articles

J Antimicrob Chemother: [Clinical efficacy and safety of remdesivir in patients with COVID-19: a systematic review and network meta-analysis of randomized controlled trials](#) (24 March 2021)

"We performed a systematic review and network meta-analysis of randomized controlled trials (RCTs) to provide updated information regarding the clinical efficacy of remdesivir in treating coronavirus disease 2019 (COVID-19).

PubMed, Embase, Cochrane Library, clinical trial registries of ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform were searched for relevant articles published up to 18 November 2020.

Five RCTs, including 13 544 patients, were included in this meta-analysis. Among them, 3839 and 391 patients were assigned to the 10 day and 5 day remdesivir regimens, respectively. Patients receiving 5 day remdesivir therapy presented greater clinical improvement than those in the control group [OR = 1.68 (95% CI 1.18–2.40)], with no significant difference observed between the 10 day and placebo groups [OR = 1.23 (95% CI 0.90–1.68)]. Patients receiving remdesivir revealed a greater likelihood of discharge [10 day remdesivir versus control: OR = 1.32 (95% CI 1.09–1.60); 5 day remdesivir versus control: OR = 1.73 (95% CI 1.28–2.35)] and recovery [10 day remdesivir versus control: OR = 1.29 (95% CI 1.03–1.60); 5 day remdesivir versus control: OR = 1.80 (95% CI 1.31–2.48)] than those in the control group. In contrast, no mortality benefit was observed following remdesivir therapy. Furthermore, no significant association was observed between remdesivir treatment and an increased risk of adverse events.

Remdesivir can help improve the clinical outcome of hospitalized patients with COVID-19 and a 5 day regimen, instead of a 10 day regimen, may be sufficient for treatment. Moreover, remdesivir appears as tolerable as other comparators or placebo."

JAMA Netw Open: [Comparison of Time to Clinical Improvement With vs Without Remdesivir Treatment in Hospitalized Patients With COVID-19](#) (24 March 2021)

"Question: Does time to clinical improvement or time to death differ among hospitalized patients treated with vs without remdesivir (alone or with corticosteroids) for coronavirus disease 2019 outside of a clinical trial?

Findings: In this multicenter comparative effectiveness research study that included 2483 consecutive admissions with a high proportion of non-White individuals, treatment with remdesivir was associated with more rapid clinical improvement than no remdesivir receipt in propensity score–matched controls. The addition of corticosteroids to remdesivir was not associated with improved time to death.

Meaning: Remdesivir administration is associated with more rapid clinical improvement than no remdesivir receipt among patients with coronavirus disease 2019."

JAMA Netw Open: [Association of Vitamin D Levels, Race/Ethnicity, and Clinical Characteristics With COVID-19 Test Results](#) (19 March 2021)

"Question: Are differences in vitamin D levels greater than levels traditionally considered sufficient (30 ng/mL) associated with having test results positive for coronavirus disease 2019 (COVID-19) in White and in Black individuals?

Findings: In this cohort study of 4638 individuals with a measured vitamin D level in the year before undergoing COVID-19 testing, the risk of having positive results in Black individuals was 2.64-fold greater with a vitamin D level of 30 to 39.9 ng/mL than a level of 40 ng/mL or greater and decreased by 5% per 1-ng/mL increase in level among individuals with a level of 30 ng/mL or greater. There were no statistically significant associations of vitamin D levels with COVID-19 positivity rates in White individuals.

Meaning: These findings suggest that randomized clinical trials to determine whether increasing vitamin D levels to greater than 30 to 40 ng/mL affect COVID-19 risk are warranted, especially in Black individuals."

JAMA: [Effect of Intermediate-Dose vs Standard-Dose Prophylactic Anticoagulation on Thrombotic Events, Extracorporeal Membrane Oxygenation Treatment, or Mortality Among Patients With COVID-19 Admitted to the Intensive Care Unit: The INSPIRATION Randomized Clinical Trial](#) (18 March 2021)

"Question: What are the effects of intermediate-dose compared with standard-dose prophylactic anticoagulation in patients with COVID-19 admitted to the intensive care unit (ICU)?

Findings: In this randomized clinical trial that included 562 patients with COVID-19 admitted to the ICU, the primary outcome (a composite of adjudicated venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or mortality within 30 days) occurred in 45.7% of patients in the intermediate-dose prophylactic anticoagulation group and 44.1% of patients in the standard-dose prophylactic anticoagulation group, a difference that was not statistically significant (odds ratio, 1.06).

Meaning: The results do not support routine empirical use of intermediate-dose prophylactic anticoagulation in unselected patients with COVID-19 admitted to the ICU."

Special Reports

ASPR TRACIE Technical Assistance Request: [\[I\]nformation on clinical presentation, disease progression, and related information from clinicians in the field treating COVID-19 patients \[pdf\]](#) (updated 10 March 2021)

"This document is a compilation of early reports and findings from published articles and clinical rounds presentations, webinars, and news articles through March 10, 2021.

Please refer to the Centers for Disease Control and Prevention's [Coronavirus Disease 2019 webpage](#) for the most up-to-date information on COVID-19 outbreak management. Please refer to the National Institutes of Health [COVID-19 Treatment Guidelines webpage](#) for up to date clinical management information.

This technical assistance (TA) response documents findings and reports from clinicians treating COVID19 patients in the U.S. We synthesized information on clinical presentation, disease progression, predictive findings, treatment pearls, and other clinical management practices that seemed consistent with other information available. It is important to note that there is only 1 year of data available on COVID19 and [new clinical patterns](#) [video; YouTube] may emerge along with new prevention and treatment patterns and the pandemic continues."

Pre-Existing Conditions and Comorbidities

Peer-Reviewed Articles

EClinicalMedicine: [Pre-existing conditions are associated with COVID-19 patients' hospitalization, despite confirmed clearance of SARS-CoV-2 virus](#) (23 March 2021)

"We conducted a retrospective analysis of 222 hospitalized COVID-19 patients to compare those that were readmitted post-viral clearance (hospitalized post-clearance cohort, n = 49) with those that were not re-admitted post-viral clearance (non-hospitalized post-clearance cohort, n = 173) between February and October 2020. In order to differentiate these two cohorts, we used neural network models for the 'augmented curation' of comorbidities and complications with positive sentiment in the Electronic Hospital Records physician notes.

In the year preceding COVID-19 onset, anemia (n = 13 [26.5%], p-value: 0.007), cardiac arrhythmias (n = 14 [28.6%], p-value: 0.015), and acute kidney injury (n = 7 [14.3%], p-value: 0.030) were significantly enriched in the physician notes of the hospitalized post-clearance cohort.

Overall, this retrospective study highlights specific pre-existing conditions that are associated with higher hospitalization rates in COVID-19 patients despite viral clearance and motivates follow-up prospective research into the associated risk factors."

Gut: [Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab](#) (22 March 2021)

"Antitumour necrosis factor (anti-TNF) drugs impair protective immunity following pneumococcal, influenza and viral hepatitis vaccination and increase the risk of serious respiratory infections. We sought to determine whether infliximab-treated patients with IBD have attenuated serological responses to SARS-CoV-2 infections.

Antibody responses in participants treated with infliximab were compared with a reference cohort treated with vedolizumab, a gut-selective anti-integrin $\alpha 4\beta 7$ monoclonal antibody that is not associated with impaired vaccine responses or increased susceptibility to systemic infections. 6935 patients were recruited from 92 UK hospitals between 22 September and 23 December 2020.

Rates of symptomatic and proven SARS-CoV-2 infection were similar between groups. Seroprevalence was lower in infliximab-treated than vedolizumab-treated patients (3.4% (161/4685) vs 6.0% (134/2250), $p < 0.0001$). Multivariable logistic regression analyses confirmed that infliximab (vs vedolizumab; OR 0.66 (95% CI 0.51 to 0.87), $p = 0.0027$) and immunomodulator use (OR 0.70 (95% CI 0.53 to 0.92), $p = 0.012$) were independently associated with lower seropositivity. In patients with confirmed SARS-CoV-2 infection, seroconversion was observed in fewer infliximab-treated than vedolizumab-treated patients (48% (39/81) vs 83% (30/36), $p = 0.00044$) and the magnitude of anti-SARS-CoV-2 reactivity was lower (median 0.8 cut-off index (0.2–5.6) vs 37.0 (15.2–76.1), $p < 0.0001$).

Infliximab is associated with attenuated serological responses to SARS-CoV-2 that were further blunted by immunomodulators used as concomitant therapy. Impaired serological responses to SARS-CoV-2 infection might have important implications for global public health policy and individual anti-TNF-treated patients. Serological testing and virus surveillance should be considered to detect suboptimal vaccine responses, persistent infection and viral evolution to inform public health policy."

Mod Pathol: [Factors associated with myocardial SARS-CoV-2 infection, myocarditis, and cardiac inflammation in patients with COVID-19](#) (17 March 2021)

"COVID-19 has been associated with cardiac injury and dysfunction. While both myocardial inflammatory cell infiltration and myocarditis with myocyte injury have been reported in patients with fatal COVID-19, clinical–pathologic correlations remain limited. The objective was to determine the relationships between cardiac pathological changes in patients dying from COVID-19 and cardiac infection by SARS-CoV-2, laboratory measurements, clinical

features, and treatments. In a retrospective study, 41 consecutive autopsies of patients with fatal COVID-19 were analyzed for the associations between cardiac inflammation, myocarditis, cardiac infection by SARS-CoV-2, clinical features, laboratory measurements, and treatments. Cardiac infection was assessed by in situ hybridization and NanoString transcriptomic profiling. Cardiac infection by SARS-CoV-2 was present in 30/41 cases: virus+ with myocarditis (n = 4), virus+ without myocarditis (n = 26), and virus- without myocarditis (n = 11). In the cases with cardiac infection, SARS-CoV-2+ cells in the myocardium were rare, with a median density of 1 cell/cm². Virus+ cases showed higher densities of myocardial CD68+ macrophages and CD3+ lymphocytes, as well as more electrocardiographic changes (23/27 vs 4/10; P = 0.01). Myocarditis was more prevalent with IL-6 blockade than with nonbiologic immunosuppression, primarily glucocorticoids (2/3 vs 0/14; P = 0.02). Overall, SARS-CoV-2 cardiac infection was less prevalent in patients treated with nonbiologic immunosuppression (7/14 vs 21/24; P = 0.02). Myocardial macrophage and lymphocyte densities overall were positively correlated with the duration of symptoms but not with underlying comorbidities. In summary, cardiac infection with SARS-CoV-2 is common among patients dying from COVID-19 but often with only rare infected cells. Cardiac infection by SARS-CoV-2 is associated with more cardiac inflammation and electrocardiographic changes. Nonbiologic immunosuppression is associated with lower incidences of myocarditis and cardiac infection by SARS-CoV-2."

JAMA Neurol: [Outcomes and Risk Factors Associated With SARS-CoV-2 Infection in a North American Registry of Patients With Multiple Sclerosis](#) (19 March 2021)

"Question: How do patients with multiple sclerosis (MS) who have COVID-19 fare and are there patient and disease characteristics associated with worse outcome?

Findings: In this registry-based cross-sectional study of 1626 North American patients with MS and COVID-19 infection, ambulatory disability, both nonambulatory and requiring assistance to walk, was independently associated with increased odds of poor clinical severity levels after adjusting for other risk factors. Other factors including older age, male sex, Black race, cardiovascular comorbidities, and corticosteroid use in the past 2 months were associated with increased odds of increasing clinical severity compared with those not requiring hospitalization or worse.

Meaning: Identification of risk factors can improve the treatment of patients with MS and COVID-19 by alerting clinicians of patients requiring more intense treatment or monitoring."

Infect Control Hosp Epidemiol: [Impact of COVID-19 Pandemic on Central Line-Associated Bloodstream Infections During the Early Months of 2020, National Healthcare Safety Network](#) (15 March 2021)

"Data reported to the Centers for Disease Control and Prevention's National Healthcare Safety Network (NHSN) were analyzed to understand the potential impact of the COVID-19

pandemic on central line-associated bloodstream infections (CLABSIs) in acute care hospitals. Descriptive analysis of the Standardized Infection Ratio (SIR) was conducted by locations, location type, geographic area, and bed size."

Reinfection, Coinfections, and Other Infectious Diseases

News in Brief

The *E. coli* outbreak from an unknown food source that caused illness in 22 and led to 1 death is officially over ([CDC](#)).

The new Ebola outbreak has been genetically traced to a survivor of the 2014-2016 West African outbreak – news that "landed like a bombshell" for researchers ([STAT](#); see also: [virological.org](#)).

Peer-Reviewed Articles

Emerg Infect Dis: [Coccidioidomycosis and COVID-19 Co-Infection, United States, 2020](#) (22 March 2021)

"We review the interaction between coronavirus disease (COVID-19) and coccidioidomycosis, a respiratory infection caused by inhalation of *Coccidioides* fungal spores in dust. We examine risk for co-infection among construction and agricultural workers, incarcerated persons, Black and Latino populations, and persons living in high dust areas. We further identify common risk factors for co-infection, including older age, diabetes, immunosuppression, racial or ethnic minority status, and smoking. Because these diseases cause similar symptoms, the COVID-19 pandemic might exacerbate delays in coccidioidomycosis diagnosis, potentially interfering with prompt administration of antifungal therapies. Finally, we examine the clinical implications of co-infection, including severe COVID-19 and reactivation of latent coccidioidomycosis. Physicians should consider coccidioidomycosis as a possible diagnosis when treating patients with respiratory symptoms. Preventive measures such as wearing face masks might mitigate exposure to dust and severe acute respiratory syndrome coronavirus 2, thereby protecting against both infections."

Lancet: [Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study](#) (17 March 2021)

"In this population-level observational study, we collected individual-level data on patients who had been tested in Denmark in 2020 from the Danish Microbiology Database and analysed infection rates during the second surge of the COVID-19 epidemic, from Sept 1 to

Dec 31, 2020, by comparison of infection rates between individuals with positive and negative PCR tests during the first surge (March to May, 2020). For the main analysis, we excluded people who tested positive for the first time between the two surges and those who died before the second surge. We did an alternative cohort analysis, in which we compared infection rates throughout the year between those with and without a previous confirmed infection at least 3 months earlier, irrespective of date. We also investigated whether differences were found by age group, sex, and time since infection in the alternative cohort analysis. We calculated rate ratios (RRs) adjusted for potential confounders and estimated protection against repeat infection as $1 - \text{RR}$.

During the first surge (ie, before June, 2020), 533 381 people were tested, of whom 11 727 (2·20%) were PCR positive, and 525 339 were eligible for follow-up in the second surge, of whom 11 068 (2·11%) had tested positive during the first surge. Among eligible PCR-positive individuals from the first surge of the epidemic, 72 (0·65% [95% CI 0·51–0·82]) tested positive again during the second surge compared with 16 819 (3·27% [3·22–3·32]) of 514 271 who tested negative during the first surge (adjusted RR 0·195 [95% CI 0·155–0·246]). Protection against repeat infection was 80·5% (95% CI 75·4–84·5). The alternative cohort analysis gave similar estimates (adjusted RR 0·212 [0·179–0·251], estimated protection 78·8% [74·9–82·1]). In the alternative cohort analysis, among those aged 65 years and older, observed protection against repeat infection was 47·1% (95% CI 24·7–62·8). We found no difference in estimated protection against repeat infection by sex (male 78·4% [72·1–83·2] vs female 79·1% [73·9–83·3]) or evidence of waning protection over time (3–6 months of follow-up 79·3% [74·4–83·3] vs ≥ 7 months of follow-up 77·7% [70·9–82·9]).

Our findings could inform decisions on which groups should be vaccinated and advocate for vaccination of previously infected individuals because natural protection, especially among older people, cannot be relied on."

J Gen Intern Med: [Comparison between Patients Hospitalized with Influenza and COVID-19 at a Tertiary Care Center](#) (18 March 2021)

"Widespread reports suggest the characteristics and disease course of coronavirus disease 2019 (COVID-19) and influenza differ, yet detailed comparisons of their clinical manifestations are lacking.

Admission rates, clinical measurements, and clinical outcomes from confirmed COVID-19 cases between March 1 and April 30, 2020, were compared with those from confirmed influenza cases in the previous five influenza seasons (8 months each) beginning September 1, 2014.

Patient demographics and medical history, mortality, incidence and duration of mechanical ventilation, incidences of vasopressor support and renal replacement therapy, and hospital and intensive care admissions.

Data was abstracted from medical records of 1052 influenza patients and 582 COVID-19 patients. An average of 210 hospital admissions for influenza occurred per 8-month season compared to 582 COVID-19 admissions over 2 months. The median weekly number of COVID-19 patients requiring mechanical ventilation was 17 (IQR: 4, 34) compared to a weekly median of 1 (IQR: 0, 2) influenza patient ($p=0.001$). COVID-19 patients were significantly more likely to require mechanical ventilation (31% vs 8%) and had significantly higher mortality (20% vs. 3%; $p<0.001$ for all). Relatively more COVID-19 patients on mechanical ventilation lacked pre-existing conditions compared with mechanically ventilated influenza patients (25% vs 4%, $p<0.001$). Pneumonia/ARDS secondary to the virus was the predominant cause of mechanical ventilation in COVID-19 patients (94%) as opposed to influenza (56%).

COVID-19 resulted in more weekly hospitalizations, higher morbidity, and higher mortality than influenza at the same hospital."

Clin Infect Dis: [Reinfection Rates among Patients who Previously Tested Positive for COVID-19: a Retrospective Cohort Study](#) (15 March 2021)

"Protection afforded from prior disease among patients with coronavirus disease 2019 (COVID-19) infection is unknown. If infection provides substantial long-lasting immunity, it may be appropriate to reconsider vaccination distribution plans.

This retrospective cohort study of one multi-hospital health system included 150,325 patients tested for COVID-19 infection via PCR from March 12, 2020 to August 30, 2020. Testing performed up to February 24, 2021 in these patients was included for analysis. The main outcome was reinfection, defined as infection ≥ 90 days after initial testing. Secondary outcomes were symptomatic infection and protection of prior infection against reinfection.

Of 150,325 patients, 8,845 (5.9%) tested positive and 141,480 (94.1%) tested negative prior to August 30. 1,278 (14.4%) of the positive patients were retested after 90 days, and 62 had possible reinfection. Of those, 31 (50%) were symptomatic. Of those with initial negative testing, 5,449 (3.9%) were subsequently positive and 3,191 of those (58.5%) were symptomatic. Protection offered from prior infection was 81.8% (95% confidence interval 76.6 to 85.8), and against symptomatic infection was 84.5% (95% confidence interval 77.9 to 89.1). This protection increased over time.

Prior infection in patients with COVID-19 was highly protective against reinfection and symptomatic disease. This protection increased over time, suggesting that viral shedding or ongoing immune response may persist beyond 90 days and may not represent true reinfection. As vaccine supply is limited, patients with known history of COVID-19 could delay early vaccination to allow for the most vulnerable to access the vaccine and slow transmission."

Travel Med Infect Dis: [Severe acute respiratory syndrome coronavirus 2 \(SARS-CoV-2\) and Middle East Respiratory Syndrome Coronavirus \(MERS-CoV\) coinfection: A unique case series](#) (13 March 2021)

"The emergence of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) had raised possibilities of coinfection with the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in countries where these two viruses were reported. In this study, we describe the clinical presentation and demographics of eight patients who were coinfecting with SARS-CoV-2 and MERS-CoV.

This is a case series of hospitalized patients admitted to intensive care units (ICUs). We collected demographics, underlying conditions, presenting symptoms and clinical outcome from the patients' medical records.

During the study period from March 14, 2020 to October 19, 2020, there was a total of 67 SARS-CoV-2 ICU admitted patients who underwent simultaneous SARS-CoV-2 and MERS-CoV testing by PCR. Of those patients, 8 (12%) tested positive for both SARS-CoV-2 and MERS-CoV. There were 6 (75%) males, the mean age \pm SD was 44.4 ± 11.8 years, and 7 (87.5%) were obese. Of the patients, 7 (87.5%) were non-smokers, 1 (12.5%) had diabetes mellitus, 1 (12.5%) had heart failure, and 1 (12.5%) had been on anti-platelet therapy. The mean hospital length of stay (LOS) was 21.1 ± 11.6 days and the average ICU LOS was 10.9 ± 6.03 days. All patients received supportive therapy and all were treated with corticosteroid. Of all the patients, 4 (50%) were discharged home and 3 (37.5%) died.

This case series is an important addition to the medical knowledge as it showed the interaction of the coinfection of SARS-CoV-2 and MERS-CoV."

Emerg Infect Dis: [Intersecting Paths of Emerging and Reemerging Infectious Diseases](#) (11 March 2021)

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) shares common clinicopathologic features with other severe pulmonary illnesses. Hantavirus pulmonary syndrome was diagnosed in 2 patients in Arizona, USA, suspected of dying from infection with SARS-CoV-2. Differential diagnoses and possible co-infections should be considered for cases of respiratory distress during the SARS-CoV-2 pandemic."

Long COVID

News in Brief

"We need to start thinking more critically — and speaking more cautiously — about long Covid" ([STAT](#)).

"Some long-haul covid-19 patients say their symptoms are subsiding after getting vaccines" ([WashPo](#)).

"Long-haulers are pushing the limits of COVID-19 vaccines: People with long COVID were left out of vaccine trials. They are now navigating the new shots on their own" ([Atlantic](#)).

"Relearning to smell after COVID-19 is its own strange experience" ([Atlantic](#)).

Long read: "The medical system should have been prepared for long COVID: COVID long haulers have been breathlessly covered, but there's nothing surprising about medically unexplained symptoms—or the reaction to them" ([Vice](#)).

Peer-Reviewed Articles

Ann Clin Transl Neurol: [Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 "long haulers"](#) (23 March 2021)

"Most SARS-CoV-2-infected individuals never require hospitalization. However, some develop prolonged symptoms. We sought to characterize the spectrum of neurologic manifestations in non-hospitalized Covid-19 "long haulers".

This is a prospective study of the first 100 consecutive patients (50 SARS-CoV-2 laboratory-positive and 50 laboratory-negative individuals) presenting to our Neuro-Covid-19 clinic between May and November 2020. Due to early pandemic testing limitations, patients were included if they met Infectious Diseases Society of America symptoms of Covid-19, were never hospitalized for pneumonia or hypoxemia and had neurologic symptoms lasting over 6 weeks. We recorded the frequency of neurologic symptoms and analyzed patient-reported quality of life measures and standardized cognitive assessments.

Mean age was 43.2±11.3 years, 70% were female and 48% were evaluated in televisits. The most frequent comorbidities were depression/anxiety (42%) and autoimmune disease (16%). The main neurologic manifestations were: "brain fog" (81%), headache (68%), numbness/tingling (60%), dysgeusia (59%), anosmia (55%), myalgias (55%), with only anosmia being more frequent in SARS-CoV-2+ than SARS-CoV-2- patients (37/50 [74%] vs (18/50 [36%]; p <0.001). Moreover, 85% also experienced fatigue. There was no correlation between time from disease onset and subjective impression of recovery. Both groups exhibited impaired quality of life in cognitive and fatigue domains. SARS-CoV-2+ patients performed worse in attention and working memory cognitive tasks compared to a demographic-matched US population (T-score 41.5 [37, 48.25] and 43 [37.5, 48.75], respectively; both p<0.01).

Non-hospitalized Covid-19 "long haulers" experience prominent and persistent "brain fog" and fatigue that affect their cognition and quality of life."

Nat Med: [Post-acute COVID-19 syndrome](#) (22 March 2021)

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the pathogen responsible for the coronavirus disease 2019 (COVID-19) pandemic, which has resulted in global healthcare crises and strained health resources. As the population of patients recovering from COVID-19 grows, it is paramount to establish an understanding of the healthcare issues surrounding them. COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations. Similarly to post-acute viral syndromes described in survivors of other virulent coronavirus epidemics, there are increasing reports of persistent and prolonged effects after acute COVID-19. Patient advocacy groups, many members of which identify themselves as long haulers, have helped contribute to the recognition of post-acute COVID-19, a syndrome characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms. Here, we provide a comprehensive review of the current literature on post-acute COVID-19, its pathophysiology and its organ-specific sequelae. Finally, we discuss relevant considerations for the multidisciplinary care of COVID-19 survivors and propose a framework for the identification of those at high risk for post-acute COVID-19 and their coordinated management through dedicated COVID-19 clinics."

JAMA: [Four-Month Clinical Status of a Cohort of Patients After Hospitalization for COVID-19](#) (17 March 2021)

"Question: What are the clinical outcomes after hospitalization for COVID-19?

Findings: Four months after hospitalization, in an uncontrolled cohort study of 478 survivors of COVID-19, at least 1 new-onset symptom was reported by telephone interview by 244 patients (51%), including fatigue in 134 of 431 (31%), cognitive symptoms in 86 of 416 (21%), and dyspnea in 78 of 478 (16%). Computed tomographic lung scan abnormalities were reported in 63% of 171 patients assessed at an ambulatory visit, mainly subtle ground-glass opacities. Fibrotic lesions were observed in 19% of these 171 patients.

Meaning: This study provides clinical status of a cohort of patients 4 months after hospitalization for COVID-19, but further research is needed to understand longer-term outcomes."

Pregnancy and Perinatal Care

News in Brief

Early data suggest vaccinated mothers pass on SARS-CoV-2 antibodies in utero and in breastmilk ([WashPo](#); see also: [JAMA Pediatr article](#), [medRxiv preprint on transplacental transfer](#), [medRxiv preprint](#) mentioned in last week's report).

Podcast: [COVID and pregnancy – what do we know?](#) (12 March 2021)

Peer-Reviewed Articles

BMC Pediatr: [Newborn antibodies to SARS-CoV-2 detected in cord blood after maternal vaccination - a case report](#) (22 March 2021)

"Maternal vaccination for Influenza and Tetanus, Diphtheria, acellular Pertussis (TDaP) have been well studied in terms of safety and efficacy for protection of the newborn by placental passage of antibodies. Similar newborn protection would be expected after maternal vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19). There is a significant and urgent need for research regarding safety and efficacy of vaccination against SARS-CoV-2 during pregnancy.

A vigorous, healthy, full-term female was born to a COVID-19 naïve mother who had received a single dose of messenger RNA (mRNA) vaccine for SARS-CoV-2 3 weeks prior to delivery. IgG cord blood antibodies were detected to SARS-CoV-2 at the time of birth.

Here, we report the first known case of an infant with SARS-CoV-2 IgG antibodies detectable in cord blood after maternal vaccination."

CMAJ: [The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis](#) (19 March 2021)

"We conducted a systematic review and meta-analysis of observational studies with comparison data on SARS-CoV-2 infection and severity of COVID-19 during pregnancy. We searched for eligible studies in MEDLINE, Embase, ClinicalTrials.gov, medRxiv and Cochrane databases up to Jan. 29, 2021, using Medical Subject Headings terms and keywords for "severe acute respiratory syndrome coronavirus 2 OR SARS-CoV-2 OR coronavirus disease 2019 OR COVID-19" AND "pregnancy." We evaluated the methodologic quality of all included studies using the Newcastle–Ottawa Scale. Our primary outcomes were preeclampsia and preterm birth. Secondary outcomes included stillbirth, gestational diabetes and other pregnancy outcomes. We calculated summary odds ratios (ORs) or weighted mean differences with 95% confidence intervals (CI) using random-effects meta-analysis.

We included 42 studies involving 438 548 people who were pregnant. Compared with no SARS-CoV-2 infection in pregnancy, COVID-19 was associated with preeclampsia (OR 1.33, 95% CI 1.03 to 1.73), preterm birth (OR 1.82, 95% CI 1.38 to 2.39) and stillbirth (OR 2.11, 95% CI 1.14 to 3.90). Compared with mild COVID-19, severe COVID-19 was strongly associated with preeclampsia (OR 4.16, 95% CI 1.55 to 11.15), preterm birth (OR 4.29, 95%

CI 2.41 to 7.63), gestational diabetes (OR 1.99, 95% CI 1.09 to 3.64) and low birth weight (OR 1.89, 95% CI 1.14 to 3.12).

COVID-19 may be associated with increased risks of preeclampsia, preterm birth and other adverse pregnancy outcomes."

Am J Perinatol: [Management and Early Outcomes of Neonates Born to Women with SARS-CoV-2 in 16 U.S. Hospitals](#) (15 March 2021)

"We solicited cases of mother–infant dyads affected by novel coronavirus disease 2019 (COVID-19) from the Better Outcomes through Research for Newborns (BORN) Network members. Using a structured case template, participating sites contributed deidentified, retrospective birth hospitalization data for neonates ≥ 35 weeks of gestation at birth with mothers who tested positive for SARS-CoV-2 before delivery. We describe demographic and clinical characteristics, clinical management, and neonatal outcomes.

Sixteen U.S. hospitals contributed 70 cases. Birth hospitalizations were uncomplicated for 66 (94%) neonates in which 4 (6%) required admission to a neonatal intensive care unit. None required evaluation or treatment for infection, and all who were tested for SARS-CoV-2 were negative ($n = 57$). Half of the dyads were colocated ($n = 34$) and 40% directly breastfed ($n = 28$). Outpatient follow-up data were available for 13 neonates, all of whom remained asymptomatic.

In this multisite case series of 70 neonates born to women with SARS-CoV-2 infection, clinical outcomes were overall good, and there were no documented neonatal SARS-CoV-2 infections. Clinical management was largely inconsistent with contemporaneous U.S. COVID-19 guidelines for nursery care, suggesting concerns about the acceptability and feasibility of those recommendations. Longitudinal studies are urgently needed to assess the benefits and harms of current practices to inform evidence-based clinical care and aid shared decision-making.

Key Points

- Birth hospitalizations were uncomplicated for late preterm and term infants with maternal COVID-19.
- Nursery management of dyads affected by COVID-19 varied between hospitals.
- Adherence to contemporaneous U.S. clinical guidelines for nursery care was low.
- Breastfeeding rates were lower for dyads roomed separately than those who were colocated."

BMJ Glob Health: [Small and sick newborn care during the COVID-19 pandemic: global survey and thematic analysis of healthcare providers' voices and experiences](#) (14 March 2021)

"The COVID-19 pandemic is disrupting health systems globally. Maternity care disruptions have been surveyed, but not those related to vulnerable small newborns. We aimed to survey reported disruptions to small and sick newborn care worldwide and undertake thematic analysis of healthcare providers' experiences and proposed mitigation strategies.

Using a widely disseminated online survey in three languages, we reached out to neonatal healthcare providers. We collected data on COVID-19 preparedness, effects on health personnel and on newborn care services, including kangaroo mother care (KMC), as well as disruptors and solutions.

We analysed 1120 responses from 62 countries, mainly low and middle-income countries (LMICs). Preparedness for COVID-19 was suboptimal in terms of guidelines and availability of personal protective equipment. One-third reported routine testing of all pregnant women, but 13% had no testing capacity at all. More than 85% of health personnel feared for their own health and 89% had increased stress. Newborn care practices were disrupted both due to reduced care-seeking and a compromised workforce. More than half reported that evidence-based interventions such as KMC were discontinued or discouraged. Separation of the mother–baby dyad was reported for both COVID-positive mothers (50%) and those with unknown status (16%). Follow-up care was disrupted primarily due to families' fear of visiting hospitals (~73%).

Newborn care providers are stressed and there is lack clarity and guidelines regarding care of small newborns during the pandemic. There is an urgent need to protect life-saving interventions, such as KMC, threatened by the pandemic, and to be ready to recover and build back better."

Children—At Home and At School

Peer-Reviewed Articles

MMWR: [COVID-19 in Primary and Secondary School Settings During the First Semester of School Reopening — Florida, August–December 2020](#) (19 March 2021)

"What is already known about this topic? Limited U.S. data have been reported regarding COVID-19 in students and school staff members as kindergarten through grade 12 (K–12) schools have reopened.

What is added by this report? COVID-19 school-related disease incidence among Florida students was correlated with community incidence in the counties observed and was highest in smaller counties, districts without mask requirements, and those that reopened

earliest after closure in March 2020. Incidence increased with the proportion of students receiving in-person instruction. Fewer than 1% of registered students were identified as having school-related COVID-19.

What are the implications for public health practice? Both community-level and school-based mitigation measures are important in limiting transmission of COVID-19; school reopening can likely be achieved without widespread student illness in K–12 settings."

MMWR: [Low SARS-CoV-2 Transmission in Elementary Schools — Salt Lake County, Utah, December 3, 2020–January 31, 2021](#) (19 March 2021)

"What is already known about this topic? Data suggest that school-associated SARS-CoV-2 transmission is low.

What is added by this report? SARS-CoV-2 testing was offered to 1,041 school contacts of 51 index patients across 20 elementary schools in Salt Lake County, Utah. In a high community transmission setting, low school-associated transmission was observed with a 0.7% secondary attack rate. Mask adherence was high, but students' classroom seats were <6 ft apart and a median of 3 ft apart.

What are the implications for public health practice? These findings add to evidence that in-person elementary schools can be opened safely with minimal in-school transmission when critical prevention strategies including mask use are implemented, even though maintaining ≥6 ft between students' seats might not be possible."

MMWR: [Pilot Investigation of SARS-CoV-2 Secondary Transmission in Kindergarten Through Grade 12 Schools Implementing Mitigation Strategies — St. Louis County and City of Springfield, Missouri, December 2020](#) (19 March 2021)

"What is already known about this topic? Many kindergarten through grade 12 (K–12) schools have implemented strategies to limit school-associated SARS-CoV-2 transmission.

What is added by this report? In 22 participating K–12 schools implementing multiple COVID-19 mitigation strategies, school-based SARS-CoV-2 secondary transmission was detected in two of 102 tested close contacts of 37 persons with COVID-19. Among 21 tested student contacts participating in a modified quarantine, all SARS-CoV-2 test results were negative.

What are the implications for public health practice? Schools implementing strategies including mask mandates, physical distancing, and increased ventilation had much lower SARS-CoV-2 transmission than in the community. K–12 schools should continue implementing these measures and following CDC isolation and quarantine guidance to minimize secondary transmission in schools."

Clin Infect Dis: [Household SARS-CoV-2 transmission and children: a network prospective study](#)
(12 March 2021)

"The role of children in household transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains uncertain. Here, we describe the epidemiological and clinical characteristics of children with COVID-19 in Catalonia (Spain) and investigate the dynamics of household transmission.

Prospective, observational, multicenter study performed during summer and school periods (1 July-31 October, 2020), in which epidemiological and clinical features, and viral transmission dynamics were analyzed in COVID-19 patients <16 years. A pediatric index case was established when a child was the first individual infected within a household. Secondary cases were defined when another household member tested positive for SARS-CoV-2 before the child. The secondary attack rate (SAR) was calculated, and logistic regression was used to assess associations between transmission risk factors and SARS-CoV-2 infections.

The study included 1040 COVID-19 patients <16 years. Almost half (47.2%) were asymptomatic, 10.8% had comorbidities, and 2.6% required hospitalization. No deaths were reported. Viral transmission was common among household members (62.3%). More than 70% (756/1040) of pediatric cases were secondary to an adult, whereas 7.7% (80/1040) were index cases. The SAR was significantly lower in households with COVID-19 pediatric index cases during the school period relative to summer ($p=0.02$), and when compared to adults ($p=0.006$). No individual or environmental risk factors associated with the SAR were identified.

Children are unlikely to cause household COVID-19 clusters or be major drivers of the pandemic even if attending school. Interventions aimed at children are expected to have a small impact on reducing SARS-CoV-2 transmission."

Clin Infect Dis: [Transmission of SARS-CoV-2 infection among children in summer schools applying stringent control measures in Barcelona, Spain](#) (12 March 2021)

"The role of children in household transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains uncertain. Here, we describe the epidemiological and clinical characteristics of children with COVID-19 in Catalonia (Spain) and investigate the dynamics of household transmission.

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Children are unlikely to cause household COVID-19 clusters or be major drivers of the pandemic even if attending school. Interventions aimed at children are expected to have a small impact on reducing SARS-CoV-2 transmission."

Mental Health and Wellness

News in Brief

Long read: "The problem is work: Pandemic parenting is impossible. American work culture is a big reason why." ([Vox](#))

Peer-Reviewed Articles

MMWR: [Association of Children's Mode of School Instruction with Child and Parent Experiences and Well-Being During the COVID-19 Pandemic — COVID Experiences Survey, United States, October 8–November 13, 2020](#) (19 March 2021)

"What is already known about the topic? COVID-19–associated schooling changes present stressors to children and parents that might increase risks to mental health and well-being.

What is added by this report? In a probability-based survey of parents of children aged 5–12 years, 45.7% reported that their children received virtual instruction only, 30.9% in-person only, and 23.4% combined virtual and in-person instruction. Findings suggest that virtual instruction might present more risks than does in-person instruction related to child and parental mental and emotional health and some health-supporting behaviors.

What are the implications for public health practice? Children not receiving full-time, in-person instruction and their parents might need additional supports to mitigate pandemic impacts."

JAMA Netw Open: [Association of Acute Symptoms of COVID-19 and Symptoms of Depression in Adults](#) (12 March 2021)

"This survey study investigates where acute coronavirus disease 2019 (COVID-19) is associated with the probability of subsequent depressive symptoms among US adults."

PLoS One: [Prevalence of depression, anxiety and post-traumatic stress disorder in health care workers during the COVID-19 pandemic: A systematic review and meta-analysis](#) (10 March 2021)

"Systematic search of EMBASE, MEDLINE, PsycINFO, Global Health, Web of Science, CINAHL, Google Scholar and the Chinese databases SinoMed, WanfangMed, CNKI and CQVIP, for studies conducted between December 2019 and August 2020 on the prevalence of depression, anxiety and PTSD in health care workers during the COVID-19 pandemic. Studies published in both English and Chinese were included.

Data on the prevalence of moderate depression, anxiety and PTSD was pooled across 65 studies involving 97,333 health care workers across 21 countries. The pooled prevalence of depression was 21.7% (95% CI, 18.3%-25.2%), of anxiety 22.1% (95% CI, 18.2%-26.3%), and of PTSD 21.5% (95% CI, 10.5%-34.9%). Prevalence estimates are also provided for a mild classification of each disorder. Pooled prevalence estimates of depression and anxiety were highest in studies conducted in the Middle-East (34.6%; 28.9%). Subgroup and meta-regression analyses were conducted across covariates, including sampling method and outcome measure.

This systematic review and meta-analysis has identified a high prevalence of moderate depression, anxiety and PTSD among health care workers during the COVID-19 pandemic. Appropriate support is urgently needed. The response would benefit from additional research on which interventions are effective at mitigating these risks."

Special Reports

Pew Research: [Many Americans continue to experience mental health difficulties as pandemic enters second year](#) (16 March 2021)

"High levels of distress are being experienced by those who say the coronavirus outbreak is a major threat to their personal financial situation (34% high distress) or to their personal health (28%). Psychological distress is especially common among adults ages 18 to 29 (32%), those with lower family incomes (31%) and those who have a disability or health condition that keeps them from participating fully in work, school, housework or other activities (36%)."

Disparities and Health Equity

News in Brief

The CDC is investing \$2.25 billion over 2 years to address COVID-19–related health disparities and advance health equity in high-risk and underserved groups ([CDC](#)).

The government is also committing \$10 billion to deal with "inequities in vaccine coverage based on race, income and geography" ([WashPo](#)).

Peer-Reviewed Articles

JAMA Netw Open: [Assessment of Disparities Associated With a Crisis Standards of Care Resource Allocation Algorithm for Patients in 2 US Hospitals During the COVID-19 Pandemic](#) (published 19 March 2021)

"Question: Is there an association of race and/or ethnicity with priority scores based on both short-term and longer-term estimated mortality used for resource allocation under crisis standards of care?

Findings: In this retrospective cohort study of 1127 patients with 5613 patient-days in 2 US hospitals, there was no significant association of race or ethnicity with priority score.

Meaning: In this study, the use of a crisis standards of care resource allocation policy based on both short-term and longer-term estimated mortality did not appear to discriminate against hospitalized patients based on self-identified race or ethnicity."

JAMA Netw Open: [Racial/Ethnic Disparities in Very Preterm Birth and Preterm Birth Before and During the COVID-19 Pandemic](#) (17 March 2021)

"Question: Was the first wave of the coronavirus disease 2019 (COVID-19) pandemic associated with exacerbated racial/ethnic disparities in preterm birth in New York City?

Findings: This cross-sectional study found that racial/ethnic disparities in very preterm birth and preterm birth among 8026 women were similar during the first wave of the COVID-19 pandemic in New York City compared with the same period the year prior.

Meaning: Monitoring of racial/ethnic disparities in adverse birth outcomes as the COVID-19 pandemic continues is warranted."

Ann Am Thorac Soc: [Association of Race and Ethnicity with COVID-19 Test Positivity and Hospitalization Is Mediated by Socioeconomic Factors](#) (15 March 2021)

"Rationale: Black race and Hispanic ethnicity are associated with increased risks for COVID-19 infection and severity. It is purported that socioeconomic factors may drive this association, but data supporting this assertion are sparse.

Objective: To evaluate whether socioeconomic factors mediate the association of race/ethnicity with COVID-19 incidence and outcomes.

Methods: We conducted a retrospective cohort study of adults tested for (cohort 1) or hospitalized with (cohort 2) COVID-19 between March 1 - July 23, 2020 at the University of Miami Hospital and Clinics. Our primary exposure was race/ethnicity. We considered socioeconomic factors as potential mediators of our exposure's association with outcomes. We used standard statistics to describe our cohorts and multivariable regression modeling to identify associations of race/ethnicity with our primary outcomes, one for each cohort, of test positivity (cohort 1) and hospital mortality (cohort 2). We performed a mediation analysis to see if household income, population density, and household size mediated the association of race/ethnicity with outcomes.

Results: Our cohorts included 15,473 patients tested (29.0% non-Hispanic White, 48.1% Hispanic White, 15.0% non-Hispanic Black, 1.7% Hispanic Black, 1.6% Other) and 295 patients hospitalized (9.2% non-Hispanic White, 56.9% Hispanic White, 21.4% non-Hispanic Black, 2.4% Hispanic Black, 10.2% Other). Among those tested, 1,256 patients (8.1%) tested positive and, of the hospitalized patients, 47 (15.9%) died. After adjustment for demographics, race/ethnicity was associated with test positivity—odds-ratio (95% CI) vs. non-Hispanic White for Non-Hispanic Black: 3.21 (2.60-3.96), Hispanic White: 2.72 (2.28-3.26), and Hispanic Black: 3.55 (2.33-5.28). Population density mediated this association (percent mediated (95% CI): 17% (11%-31%)), as did median income (27% (18%-52%)), and household size (20% (12%-45%)). There was no association between race/ethnicity and mortality although this analysis was underpowered.

Conclusions: Black race and Hispanic ethnicity are associated with an increased odds of COVID-19 positivity. This association is substantially mediated by socioeconomic factors."

Preparedness and Planning

News in Brief

"After U.S. failures on Covid, Congress is working to prepare America to fight the next pandemic" ([STAT](#)).

Peer-Reviewed Articles

JAMA Netw Open: [US Hospital Capacity Managers' Experiences and Concerns Regarding Preparedness for Seasonal Influenza and Influenza-like Illness](#) (19 March 2021)

"Question: What were US hospitals' experiences and the views of hospital capacity managers regarding response and preparedness activities during the 2017-2018 influenza epidemic?

Findings: In this qualitative study using semistructured telephone interviews with 53 key hospital capacity personnel at 53 hospitals throughout the US, perceived strain on hospital resources was almost universally reported. Participants described a range of hospital responses to seasonal influenza but indicated that future pandemic planning was not a high priority.

Meaning: The findings suggest that, during the 2017-2018 influenza epidemic, there were vulnerabilities in the US health care system, including a lack of planning for future pandemic events, which may have implications for public health planning given the ongoing coronavirus disease 2019 pandemic."

J Travel Med: [Border control and SARS-CoV-2: an opportunity for generating highly policy-relevant, real-world evidence](#) (12 March 2021)

"We propose a study type that would contribute to the evidence base related to border control measures. Over a study period during which arriving travellers are quarantined, repeated testing and/or screening at regular intervals would provide real-world data on the relative and combined effects of various screening and testing measures."

Testing and Diagnostics

News in Brief

The FDA has granted marketing for the BioFire Respiratory Panel 2.1 diagnostic test ([FDA](#)).

Peer-Reviewed Articles

JAMA Netw Open: [Association of Clinical, Biological, and Brain Magnetic Resonance Imaging Findings With Electroencephalographic Findings for Patients With COVID-19](#) (15 March 2021)

"Question: Can electroencephalography (EEG), combined with clinical, biological, and magnetic resonance imaging (MRI) analyses, help to better characterize patients with neurologic coronavirus disease 2019 (COVID-19) and diagnose specific COVID-19–related encephalopathy?

Findings: Neurologic manifestations, biological findings, EEG findings, and brain MRI images were analyzed in a cohort study of 78 adult patients with COVID-19. Nine patients had no identified cause of brain injury, as revealed by biological and MRI findings; their injury was defined as COVID-19–related encephalopathy.

Meaning: This study suggests that, although neurologic manifestations, EEG findings, and MRI findings may appear heterogeneous and nonspecific, multimodal monitoring may better identify patients with COVID-19–related encephalopathy and guide treatment strategy."

J Nippon Med Sch: [Indicators of Acute Kidney Injury as Biomarkers to Differentiate Heatstroke from Coronavirus Disease 2019: A Retrospective Multicenter Analysis](#) (11 March 2021)

"Coronavirus disease 2019 (COVID-19) and heat-related illness are systemic febrile diseases. These illnesses must be differentiated during a COVID-19 pandemic in summer. However, no studies have compared and distinguished heat-related illness and COVID-19. We compared data from patients with early heat-related illness and those with COVID-19.

This retrospective observational study included 90 patients with early heat-related illness selected from the Heatstroke STUDY 2017-2019 (nationwide registries of heat-related illness in Japan) and 86 patients with laboratory-confirmed COVID-19 who had fever or fatigue and were admitted to one of two hospitals in Tokyo, Japan.

Among vital signs, systolic blood pressure (119 vs. 125 mm Hg, $p = 0.02$), oxygen saturation (98% vs. 97%, $p < 0.001$), and body temperature (36.6°C vs. 37.6°C, $p < 0.001$) showed significant between-group differences in the heatstroke and COVID-19 groups, respectively. The numerous intergroup differences in laboratory findings included disparities in white blood cell count ($10.8 \times 10^3/\mu\text{L}$ vs. $5.2 \times 10^3/\mu\text{L}$, $p < 0.001$), creatinine (2.2 vs. 0.85 mg/dL, $p < 0.001$), and C-reactive protein (0.2 vs. 2.8 mg/dL, $p < 0.001$), although a logistic regression model achieved an area under the curve (AUC) of 0.966 using these three factors. A Random Forest machine learning model achieved an accuracy, precision, recall, and AUC of 0.908, 0.976, 0.842, and 0.978, respectively. Creatinine was the most important feature of this model.

Acute kidney injury was associated with heat-related illness, which could be essential in distinguishing or evaluating patients with fever in the summer during a COVID-19 pandemic."

Misinformation/Disinformation

News in Brief

"'Lying through truth': misleading facts fuel vaccine misinformation" ([NPR](#)).

Special Reports

JHCHS: [National Priorities to Combat Misinformation and Disinformation for COVID-19 and Future Public Health Threats: A Call for a National Strategy](#) (23 March 2021)

"The COVID-19 pandemic has shown that health-related misinformation and disinformation can dangerously undermine the response to a public health crisis. Contradictory messaging and active subversion have reduced trust in public health responders, increased belief in false medical cures, and politicized public health measures aimed at curbing transmission of the disease. Setbacks in the COVID-19 response have highlighted that health-related misinformation or disinformation can lead to more infections, deaths, disruption, and disorganization of the effort. The public health response and communication environment in the United States have been disrupted by significant distrust in government, exacerbated by confusing and conflicting messages from leaders. As a result, information voids have developed, easily filled by false or misleading information and directly targeted by perpetrators of disinformation. Taken together, the spread and consequence of public health misinformation and disinformation can lead to a range of outcomes that have national security implications and require effective response"

Pillar 1: Intervene against false and damaging content as well as the sources propagating it

Pillar 2: Promote and ensure the abundant presence and dissemination of factual information

Pillar 3: Increase the public's resilience to misinformation and disinformation

Pillar 4: Ensure a whole-of-nation response through multisector and multiagency collaboration"

Statistics

Global

26 MAR 2021: 125,629,394 confirmed cases and 2,757,473 deaths in 192 countries/regions

19 MAR 2021: 122,063,523 confirmed cases and 2,695,511 deaths in 192 countries/regions

12 MAR 2021: 118,719,900 confirmed cases and 2,632,147 deaths in 192 countries/regions

05 MAR 2021: 115,760,047 confirmed cases and 2,571,789 deaths in 192 countries/regions

United States*

top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	30,081,432	3,653,168	2,769,605	2,027,429	1,825,069	1,229,806
Deaths	546,830	58,434	47,822	32,957	49,790	23,442

*see [census.gov](https://www.census.gov) for current US Population data; NA: not all data available

[JHU CSSE](https://www.jhu-csse.org) as of 1000 EDT 26 March 2021

Virginia is ranked 17th in cases and 17th in deaths (12th in population).

Virginia	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	612,062	19,319	9,371	12,447	15,911	8,239	7,307	32,799
Hospitalizations	26,144	901	325	351	884	618	417	1,397
Deaths	10,154	266	150	204	235	168	174	358

[VA DOH](https://www.vahhs.org) as of 1000 EDT 26 March 2021